AWARD NUMBER: W81XWH-14-1-0025

TITLE: Effect of Prazosin and Naltrexone on Script Induced Alcohol Craving in Veterans with Alcohol Use Disorders with and without Co-occurring PTSD

PRINCIPAL INVESTIGATOR: Tracy Simpson, PhD

CONTRACTING ORGANIZATION: Seattle Institute for Biomedical and Clinical Research
Seattle, WA 98108

REPORT DATE: January 2016

TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

# REPORT DOCUMENTATION PAGE

*Form Approved*
*OMB No. 0704-0188*



| 1. REPORT DATE | 2. REPORT TYPE | 3. DATES COVERED |
|---|---|---|
| January 2016 | Annual | 4 Dec 2014 - 3 Dec 2015 |

**4. TITLE AND SUBTITLE:**

**Effect of Prazosin and Naltrexone on Script Induced Alcohol Craving in Veterans with Alcohol Use Disorders with and without Co-occurring PTSD**

**5a. CONTRACT NUMBER**

**5b. GRANT NUMBER**
W81XWH-14-1-0025

**5c. PROGRAM ELEMENT NUMBER**

**6. AUTHOR(S)**
Tracy Simpson, PhD

E-Mail: Tracy.Simpson@va.gov

**5d. PROJECT NUMBER**

**5e. TASK NUMBER**

**5f. WORK UNIT NUMBER**

**7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)**
Seattle Institute for Biomedical and Clinical Research
1660 S Columbia Way, S-151F, Seattle, WA 98108-1532

**8. PERFORMING ORGANIZATION REPORT NUMBER**

**9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)**

U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

**10. SPONSOR/MONITOR'S ACRONYM(S)**

**11. SPONSOR/MONITOR'S REPORT NUMBER(S)**

**12. DISTRIBUTION / AVAILABILITY STATEMENT**

Approved for Public Release; Distribution Unlimited

**13. SUPPLEMENTARY NOTES**

**14. ABSTRACT**

**Background:** Military personnel are at risk for developing hazardous drinking patterns post-deployment that can negatively impact their health and psychiatric stability. This phenomenon is compounded by the fact that despite recent gains in establishing effective pharmacological and behavioral treatments for alcohol use disorders (AUD), nonremittance and relapse remain major problems for those with AUDs. One individual factor that is strongly associated with continued problematic use and relapse is craving. Three different types of craving have been hypothesized, reward, relief, and obsessive, and each is postulated to be mediated by different neurological substrates. The neural networks postulated to subserve reward and relief craving receive afferents from and project to noradrenergic neurons in non-human primates and humans express $\alpha_1$ adrenergic receptors. Given the interplay of the noradrenergic system with craving-related brain systems, blocking $\alpha_1$ receptors with the noradrenergic antagonist, prazosin, theoretically has the potential to modulate reward and relief craving.

**Objective/Hypotheses:** The overarching objective of the study is to evaluate whether prazosin alone and/or in conjunction with naltrexone is effective at reducing reward and relief craving for alcohol among veterans with an AUD in both a human laboratory context and in their day-to-day lives via daily symptom telephone monitoring using Interactive Voice Response (IVR). The proposed study also seeks to evaluate whether specific individual characteristics, including PTSD status, moderate medication response.

**15. SUBJECT TERMS** Alcohol Drinking, Drinking Behavior, Naltrexone, Prazosin, Adrenergic Agents, Adrenergice Antagonists, Adrenergic alpha-1 receptor antagonists, Adrenergic alpha-antagonists, Antihypertensive agents, Narcotic antagonists, Therapeutic uses

| 16. SECURITY CLASSIFICATION OF: | | | 17. LIMITATION OF ABSTRACT | 18. NUMBER OF PAGES | 19a. NAME OF RESPONSIBLE PERSON |
|---|---|---|---|---|---|
| | | | | | USAMRMC |
| a. REPORT | b. ABSTRACT | c. THIS PAGE | | | 19b. TELEPHONE NUMBER *(include area code)* |
| Unclassified | Unclassified | Unclassified | Unclassified | | |

1. **INTRODUCTION:** Narrative that briefly (one paragraph) describes the subject, purpose and scope of the research.

Recently deployed Veterans are at risk of developing hazardous drinking patterns post-deployment. Craving is strongly associated with continued problematic use and relapse. The noradrenergic system subserves craving-related brain systems. Blocking α1 receptors with the noradrenergic antagonist, prazosin, has the potential to modulate craving. 120 Veterans with an alcohol use disorder (AUD) will be randomized to receive prazosin, naltrexone, both medications, or placebo for 3 weeks. The purpose of this study is to see whether the drugs prazosin and naltrexone will decrease alcohol cravings and drinking in individuals who have problems with alcohol and have used alcohol at risky levels in the past 90 days.

2. **KEYWORDS:** Provide a brief list of keywords (limit to 20 words).

Alcohol Drinking
Drinking Behavior
Alcohol Craving
Naltrexone
Prazosin
Adrenergic Agents
Adrenergic Antagonists
Adrenergic alpha-1 Receptor Antagonists
Adrenergic alpha-Antagonists
Antihypertensive Agents
Cardiovascular Agents
Central Nervous System Agents
Molecular Mechanisms of Pharmacological Action
Narcotic Antagonists
Neurotransmitter Agents
Peripheral Nervous System Agents
Pharmacologic Actions
Physiological Effects of Drugs
Sensory System Agents
Therapeutic Uses

3. **ACCOMPLISHMENTS:**

- **What were the major goals of the project?**
  See beneath for the study's scope of work table which lists major project goals.
- **What was accomplished under these goals**
  All of the preparatory tasks were completed in advance of study recruitment, participant enrollment and randomization.
  - Task 1: We obtained all required local IRB approvals and met conditions required by the DoD to start subject enrollment, including a mid-treatment urine pregnancy test and the addition of Dr. Reoux as safety monitor to our HIPAA form. We gained local approval of these DoD required changes in a protocol amendment on 10/16/14. We were unable to obtain a certificate of confidentiality due to conflicts between the VA handbook and NIH issuing rules. Per VA policy we are required to enter specific study information into a participant's medical record, including study title and medication names. NIH requires this information to be withheld from medical records for the issuance of a certificate of confidentiality.

- Task 2: The study RA has been hired and employed through SIBCR on various local studies for the past three years. SIBCR can provide an employment confirmation letter if required.
- Task 3: Research pharmacist Amy Shen procures bulk medications for us. The medications are compounded by pharmacist Roland Lopez at Kelley-Ross compounding pharmacy.
- Task 4: Included with this report you will find email confirmation that our research pharmacist, Amy Shen, is keeping our randomization logs and dispensing study medications.
- Task 5: A copy of our research request for laboratory testing is included. It details the type of labs and costs we order for the study.
- Task 6: Final case report forms were sent to DoD upon local VA approval to conduct the study. If you need current copies of our case report forms we would be happy to provide them.
- Task 7: We were approved by the VA IRB to use the PTSD Symptom Severity Interview (PSS-I) by Edna Foa rather than the CAPS. The PSS-I has very good agreement with the CAPS, takes approximately half the time, and the use of this measure has been indicated in all of the protocols that DoD has reviewed. Dr. Simpson has evaluated the clinician's reliability in diagnosing PTSD via the PSS-I, which was found to be excellent, for the first 10 study participants as well as in prior studies using this measure. Should the DoD determine that the use of the PSS-I is not acceptable, we will switch over and will use the CAPS. Co-Investigator Dr. Matthew Jakupcak is adept at training clinicians on the CAPS and can do so for this study if needed. While it does require rewording of the SOW, this is not a significant change in the aims of the approved research project.
- Task 8: IVR system is functional.
- Task 9: Local VA and community recruitment strategies are being utilized to attract potential participants. VA recruitment strategies include flyers, monitor ads, clinician referrals and study letters to Veterans identified as likely eligible via our VINCI data pull. Community recruitment includes reaching out to local Veteran organizations (e.g., DAV), posting at colleges and universities and craigslist ads. We are also exploring the use of a web-based recruitment company (Autocruitment), though at the time of this revision it does not appear that the VA IRB is going to approve it.
- Task 10: SIBCR confirmation of participant payment system set-up is verified by our senior grants and contracts manager, Rebecca Walker. See attached for Rebecca's email.
- Task 11: The recruitment methods listed in task 9 are currently being used to attract participants.
- Task 12: All nine participants who were randomized before this report successfully completed the study as of 1/4/2016. Please note that although we had updated the recruitment stipulations to include all Veterans (and not just OIF/OEF Veterans) in

all of our human subjects material, we had not indicated this change in previous versions of the Statement of Work. This has now been corrected in the version below and we are also noting that we would like to extend recruitment to National Guard/Reserve members. The addition of Guard/Reserve members has been deemed acceptable to Drs. Kiselycznyk and Hoover and we have submitted a VA IRB modification to make this change.

- Task 13: Data are being entered and cleaned as we go. IVR databases are cleaned and maintained. The data from the majority of our measures are currently entered in excel files.
- Task 15: Quarterly and annual reports are completed as required by study staff.

Please note, the Statement of Work below reflects the original document submitted to DoD with the issues noted above indicated with tracked changes. A "clean" updated version is immediately below.

| | | | | | |
|---|---|---|---|---|---|
| **Specific Aim 1:** To compare the effects of prazosin only, naltrexone only, and their combination to placebo control on reward oriented and relief oriented alcohol craving elicited by personalized imaginal scripts in a human laboratory setting. | | | | | |
| **Specific Aim 2:** To determine the effect of the four medication conditions on day-to-day reports of alcohol craving and drinking motives via daily telephone IVR. | | | | | |
| **Specific Aim 3:** Explore whether PTSD status moderates medication response. | | | | | |
| Year: | 1 | 2 | 3 | 4 | |
| **Preparatory Tasks** | | | | | |
| Task 1: Obtain all necessary regulatory approvals (IRB, R&D, biohazard, ~~NIH Certificate of Confidentiality~~) | X | | | | |
| Task 2: Hire research staff (recruit study RA; study clinician is already in lab) | X | | | | |
| Task 3: Purchase medication; have study medications compounded | X | | | | |
| Task 4: Set up pharmacy dispensing, including randomization protocol | X | | | | |
| Task 5: Set up agreement with VA laboratory for blood and urine assays | X | | | | |
| Task 6: Finalize case report forms | X | | | | |
| Task 7: Train clinician on ~~Clinician Administered PTSD Scale~~PTSD Symptom Severity Interview; establish reliability | X | | | | |
| Task 8: Work with Data Systems Inc. to program IVR system | X | | | | |
| Task 9: Set up recruitment systems | X | | | | |
| Task 10: Set up participant payment and purchase order systems with SIBCR | X | | | | |
| ***Preparatory Milestones:*** Tasks 1 - 10 will be completed by the end of month 6 | | | | | |
| **Recruitment and Retention Tasks** | | | | | |
| Task 11: Initiate recruitment and retention efforts | | X | X | | |
| Task 12: Recruit and retain ~~OIF/OEF~~ Veterans- and National Guard/Reserve Members with an AUD and recent alcohol craving. | | X | X | | |
| ***Recruitment and Retention Milestones:*** | | | | | |
| • By the end of Year 1 20 ~~OIF/OEF~~ Veterans and NG/R members will | | | | | |

| | | | | | |
|---|---|---|---|---|---|
| have been recruited<br>• By the end of Year 2 60 ~~OIF/OEF Veterans~~ Veterans and NG/R members will have been recruited<br>• By the end of Year 3 100 ~~OIF/OEF~~ Veterans and NG/R members will have been recruited<br>• At the end of the first 6 months of Year 4 the total sample of 120 ~~OIF/OEF~~ Veterans and NG/R members will be recruited | | | | | |
| **Data Cleaning, Analysis, Manuscript, and Report Tasks** | | | | | |
| Task 13: Enter and clean study data (lab values, adverse events, self-report data, IVR data) | | X | X | | |
| Task 14: Perform analyses germane to Aims 1, 2, and 3 | | | | | |
| Task 15: Write and submit necessary reports to DoD | X | | X | | |
| Task 16: Write and submit manuscripts | | | | | |
| ***Data Cleaning, Analysis, Manuscript, and Report Milestones***: Tasks 13 through 16 will be completed by the end of the grant period. | | | | | |

**Comments continued:** In order receive full approval to start recruitment we obtained VAPSHCS and DoD approval of our second protocol modification. We received the approval of DoD initiated changes, and ultimately permission to enroll participants, on 10/16/14. The late 2015 beginning of our enrollment, coupled with a delay in receiving the results of our data access request, a list of likely eligible Veterans, have prevented us from achieving our year goal of enrolling 20 participants. As of 1/4/2015, 9 participants have been randomized and successfully completed the study.

Statement of Work with changes accepted:

| | | | | |
|---|---|---|---|---|
| **Specific Aim 1:** To compare the effects of prazosin only, naltrexone only, and their combination to placebo control on reward oriented and relief oriented alcohol craving elicited by personalized imaginal scripts in a human laboratory setting. | | | | |
| **Specific Aim 2:** To determine the effect of the four medication conditions on day-to-day reports of alcohol craving and drinking motives via daily telephone IVR. | | | | |
| **Specific Aim 3:** Explore whether PTSD status moderates medication response. | | | | |
| Year: | 1 | 2 | 3 | 4 |
| **Preparatory Tasks** | | | | |
| Task 1: Obtain all necessary regulatory approvals (IRB, R&D, biohazard,) | X | | | |
| Task 2: Hire research staff (recruit study RA; study clinician is already in lab) | X | | | |
| Task 3: Purchase medication; have study medications compounded | X | | | |
| Task 4: Set up pharmacy dispensing, including randomization protocol | X | | | |
| Task 5: Set up agreement with VA laboratory for blood and urine assays | X | | | |
| Task 6: Finalize case report forms | X | | | |
| Task 7: Train clinician on PTSD Symptom Severity Interview; establish reliability | X | | | |
| Task 8: Work with Data Systems Inc. to program IVR system | X | | | |
| Task 9: Set up recruitment systems | X | | | |
| Task 10: Set up participant payment and purchase order systems with SIBCR | X | | | |

| | | | | | | |
|---|---|---|---|---|---|---|
| ***Preparatory Milestones:*** Tasks 1 - 10 will be completed by the end of month 6 | | | | | | |
| **Recruitment and Retention Tasks** | | | | | | |
| Task 11: Initiate recruitment and retention efforts | | X | X | | | |
| Task 12: Recruit and retain Veterans and National Guard/Reserve Members with an AUD and recent alcohol craving. | | X | X | | | |
| ***Recruitment and Retention Milestones:*** | | | | | | |
| • By the end of Year 1 20 Veterans and NG/R members will have been recruited | | | | | | |
| • By the end of Year 2 60 Veterans and NG/R members will have been recruited | | | | | | |
| • By the end of Year 3 100 Veterans and NG/R members will have been recruited | | | | | | |
| • At the end of the first 6 months of Year 4 the total sample of 120 Veterans and NG/R members will be recruited | | | | | | |
| **Data Cleaning, Analysis, Manuscript, and Report Tasks** | | | | | | |
| Task 13: Enter and clean study data (lab values, adverse events, self-report data, IVR data) | | X | X | | | |
| Task 14: Perform analyses germane to Aims 1, 2, and 3 | | | | | | |
| Task 15: Write and submit necessary reports to DoD | X | | X | | | |
| Task 16: Write and submit manuscripts | | | | | | |
| ***Data Cleaning, Analysis, Manuscript, and Report Milestones***: Tasks 13 through 16 will be completed by the end of the grant period. | | | | | | |

- **What opportunities for training and professional development has the project provided?**

  Nothing to report

- **How were the results disseminated to communities of interest?**

  Nothing to report

- **What do you plan to do during the next reporting period to accomplish the goals?**

  *We have been unable to meet our goal of enrolling 20 participants in our first full year of recruitment.* In the next reporting period we plan to hone recruitment strategies by strategically recruiting likely eligible vets through our addiction treatment clinic, through community veteran organizations, continuing with our contact of veterans identified as likely candidates through the results of our data access request and through VA wide listserve emails. We have also requested a modest change to our inclusion criteria (pending with the IRB) to allow people who have engaged in steady hazardous drinking for at least two weeks of the last month but who may or may not have consumed alcohol in the last two weeks. This stipulation of very recent drinking being necessary has resulted in 16 of

otherwise eligible participants being screened out. Additionally, we would like to start recruiting National Guard/Reserve members because it has been much more difficult than anticipated to find Veteran participants that meet our study criteria. Specifically, we are having difficulty finding veterans with alcohol use disorders currently drinking at hazardous levels or veterans who are not currently taking naltrexone or prazosin. Although we had hoped to include civilians in the study to increase the recruitment pool, following discussion with DoD officials, it was decided to not move forward with this option.

4. **IMPACT:** This component is used to describe ways in which the work, findings, and specific products of the project have had an impact during this reporting period. Describe distinctive contributions, major accomplishments, innovations, successes, or any change in practice or behavior that has come about as a result of the project relative to:

    - **What was the impact on the development of the principal discipline(s) of the project?**

      Nothing to report

    - **What was the impact on other disciplines?**

      Nothing to report

    - **What was the impact on technology transfer?**

      Nothing to report

    - **What was the impact on society beyond science and technology?**

      Nothing to report

5. **CHANGES/PROBLEMS:** The Project Director/Principal Investigator (PD/PI) is reminded that the recipient organization is required to obtain prior written approval from the awarding agency Grants Officer whenever there are significant changes in the project or its direction. If not previously reported in writing, provide the following additional information or state, "Nothing to Report," if applicable:

    - **Changes in approach and reasons for change**

      Nothing to report

    - **Actual or anticipated problems or delays and actions or plans to resolve them**

      It took months to receive our final list of veterans that likely meet study criteria via our data access request. We see this as a major recruitment method for the current study,

and as such plan on mailing these veterans with increased frequency during the upcoming study year.

- **Changes that had a significant impact on expenditures**

  The unanticipated waiting period for human subject approval and data access request left us well under our projected expenditures for the first year of study activity. We expect to use these funds for their allocated purposes later in the project.

- **Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents**

  Nothing to report

6. **PRODUCTS:** List any products resulting from the project during the reporting period. Examples of products include:

   - **Publications, conference papers, and presentations**

     Nothing to report

   - **Website(s) or other Internet site(s)**

     Nothing to report

   - **Technologies or techniques**

     Nothing to report

   - **Inventions, patent applications, and/or licenses**

     Nothing to report

   - **Other Products**

     Nothing to report

7. **PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS**

   - **What individuals have worked on the project?**

Provide the following information for: (1) PDs/PIs; and (2) each person who has worked at least one person month per year on the project during the reporting period, regardless of the source of compensation (a person month equals approximately 160 hours of effort).

- Provide the name and identify the role the person played in the project. Indicate the nearest whole person month (Calendar, Academic, Summer) that the individual worked on the project. Show the most senior role in which the person worked on the project for any significant length of time. For example, if an undergraduate student graduated, entered graduate school, and continued to work on the project, show that person as a graduate student, preferably explaining the change in involvement.

  Describe how this person contributed to the project and with what funding support. If information is unchanged from a previous submission, provide the name only and indicate "no change".

| **Individuals Working on this Project** | |
|---|---|
| Name: | Tracy Simpson, PhD |
| Project Role: | PI |
| Nearest person month worked: | 1.8 |
| Contribution: | PI |
| | |
| Name: | Andrew Saxon, MD |
| Project Role: | Co-PI |
| Nearest person month worked: | 1.2 |
| Contribution: | PI |
| | |
| Name: | Robert Lyons |
| Project Role: | Research Coordinator |
| Nearest person month worked: | 12 |
| Contribution: | Participant Recruitment and Regulatory Duties |
| | |
| Name: | Dana Tell, ARNP |
| Project Role: | Study Clinician |
| Nearest person month worked: | 6 |
| Contribution: | Performs in-person participant visits |

  - **Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?**

    Nothing to report

  - **What other organizations were involved as partners?**

    Nothing to report

8. **SPECIAL REPORTING REQUIREMENTS:** See included quad chart.

# Effect of Prazosin and Naltrexone on Script Induced Alcohol Craving in Veterans with Alcohol Use Disorders with and without Co-occurring PTSD

11152009 / W81XWH-14-1-0025

**PI:** Tracy Simpson, PhD / Andrew Saxon, MD **Org:** Seattle Institute for Biomedical and Clinical Research **Award Amount:** $802,000

## Approach

Recently deployed Veterans are at risk of developing hazardous drinking patterns post-deployment. Craving is strongly associated with continued problematic use and relapse. The noradrenergic system subserves craving-related brain systems. Blocking α1 receptors with the noradrenergic antagonist, prazosin, has the potential to modulate craving.

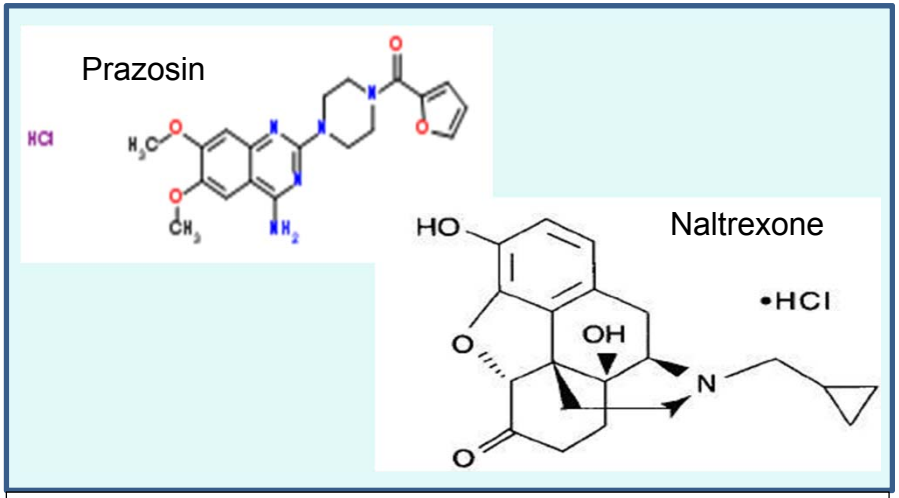
120 Veterans with an alcohol use disorder (AUD) will be randomized to receive prazosin, naltrexone, both medications, or placebo for 3 weeks. Craving will be assessed through daily monitoring and a laboratory based craving induction paradigm.

## Study Aims

**Specific Aim 1:** To compare the effects of prazosin only, naltrexone only, and their combination to placebo control on reward oriented and relief oriented alcohol craving elicited in a human laboratory setting.

**Specific Aim 2:** To determine the effect of the four medication conditions on day-to-day reports of alcohol craving and drinking motives.

**Specific Aim 3:** To explore whether PTSD status moderates medication response.




Accomplishments: Obtained local IRB and R&D approvals; undergoing DoD IRB review; research staff hired; daily monitoring system constructed; pharmacy & lab interfaces established; compounding pharmacy interface established.

## Timeline and Cost

| Activities | CY 13 | 14 | 15 | 16 | 17 |
|---|---|---|---|---|---|
| Preparatory Tasks | | | | | |
| Recruitment/Retention | | | | | |
| Enter and clean study data | | | | | |
| Analyze data for Aims 1, 2 & 3; write and submit manuscripts | | | | | |
| **Estimated Budget ($K)** | | **$139k** | **$207k** | **$212k** | **$244** |

**Budget Expenditure to Date:** Projected Expenditure: $207,353
Actual Expenditure: $207,275

**Goals/Milestones** ☑☑☑ ☐☐☐

**CY14 Goals**
- ☑ Obtain all necessary regulatory approvals
- ☑ Prepare staff; compound meds; set up lab and IVR.
- ☑ Initiate recruitment and retention efforts
- ☐ 20 Veterans recruited by the end of year 1

**CY15 Goals**
- ☐ 60 Veterans recruited by the end of year 2
- ☑ Enter and clean study data

**CY16 Goals**
- ☐ 100 Veterans recruited by the end of year 3
- ☐ Enter and clean study data

**CY17 Goals**
- ☐ 120 Veterans recruited by half way through year 4
- ☐ Perform date analyses for Aims 1, 2, and 3.
- ☐ Write and submit manuscripts

**Comments/Challenges/Issues/Concerns**

- We experienced delays with our IRB in securing final approval for changes requested by DoD in addition to delays in receiving an approved list of likely eligible Veterans, which delayed recruitment.
- The above mentioned delays also resulted in our being below projected expenditure.

**Updated:** (N/A)

**From:** Shen, Amy C
**To:** Lyons, Robert C.
**Subject:** RE: Proof of Randomization and Dispensing
**Date:** Tuesday, April 05, 2016 4:31:37 PM

---

You are asking about PaN study?! Yes, I maintaining randomization logs and dispensing study drugs according to randomization.

Thanks,

Amy Shen, RPh, MS
Investigational Drug Program Manager
VA PSHCS

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**From:** Lyons, Robert C.
**Sent:** Tuesday, April 05, 2016 4:17 PM
**To:** Shen, Amy C
**Subject:** Proof of Randomization and Dispensing

Good Afternoon Amy,

Our study sponsor would like proof that you are maintaining the randomization logs and dispensing meds to participants. Would you be able to provide us with confirmation that you are indeed responsible for the aforementioned tasks?

Thanks,
Robbie

| | |
|---|---|
| **From:** | Rebecca Walker |
| **To:** | Lyons, Robert C. |
| **Cc:** | Simpson, Tracy L |
| **Subject:** | [EXTERNAL] Subject Payment and Purchase Orders ST119 (W81XWH-14-1-0025/11152009/A18052) |
| **Date:** | Tuesday, April 12, 2016 8:12:04 AM |

---

Dear Robbie,

Participant payments for this project are actively being made via purchase order in accordance with SIBCR's Purchasing Policy and standard subject payment procedures. We have made more than 50 subject payments since January 2015 and the study also has access to petty cash for subjects who do not feel comfortable with reimbursement by check (last batch issued Dec 2014).

Appropriate language is included in the human subjects consent form or Health Insurance Portability and Accountability Act (HIPAA) addendum to notify the participant that the individual's Protected Health Information (PHI) will be released to SIBCR in order to process such payments. SIBCR is listed on the version of the consent form we have on file – section 7, page 16 – as an entity that receives personal information.

Best regards,
Rebecca Walker

_____

Ms. Rebecca E. Walker - Senior Grants and Contracts Manager - SIBCR - www.sibcr.org - rebecca@sibcr.org - +1 206 204 6186

# RESEARCH REQUEST for Laboratory Testing

Title of Project: **Effect of Prazosin and Naltrexone on Script Induced Alcohol Craving in Veterans with Alcohol Use Disorders with and without Co-occurring PTSD**

Billing information (Account number) _____ST-119_____

Principal Investigator: Tracy Simpson, PhD  Today's Date: 9/12/14

Human subject approval:  YES ___x___NO _____Pending_____

Funding by [VA]____[NIH] _____ [OTHER- please specify] Department of Defense_____

Duration of project (month/year): __4 years _ FROM ____10/2014_____ TO_____10/2018_____

Contact Person: _____Robert Lyons_____ Telephone number:____206-716-5740_____

Report Critical Values to: _Andrew Saxon, MD__ _____ Telephone number:_206-277-3770___

| INVESTIGATOR COMPLETES (# OF TESTS/YEAR) | | | | | LAB COMPLETES | | | |
|---|---|---|---|---|---|---|---|---|
| TEST NAME | CPTCode (optional) | Year 1 | Year 2 | Year 3 | COST PER TEST | Year 1 | Year 2 | Year 3 |
| Qualitative HCG | 81025 | | | | $5.13 | | | |
| Sample – Urine, spot<br>UA-Routing Screen | 81003 | | | | $3.06 | | | |
| Sample – Blood, Lavender<br>CBC | 85025 | | | | $10.61 | | | |
| Sample – Serum, Gold<br>o Chem 7 | 80053 | | | | $11.64 | | | |
| Sample – Serum, Gold<br>Tot Bilirubin | | | | | | | | |
| Sample – Serum, Gold<br>o Protein | | | | | | | | |
| Sample – Serum, Gold<br>o Albumin | | | | | | | | |
| Sample – Serum, Gold<br>o LDH Total | | | | | | | | |
| Sample – Serum, Gold<br>o SGOT | | | | | | | | |
| Sample – Serum, Gold<br>o SGPT | | | | | | | | |

# RESEARCH REQUEST for Laboratory Testing

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Sample – Serum, Gold<br>o SGGT | | | | | | | | |
| Sample – Serum, Gold<br>o Alkaline Phosphatase | | | | | | | | |
| | | | | | | | | |
| | | | | | TOTAL | $30.44 | | |

Investigator's Signature 9/15/14 Date

Chief, P&LMS RN.CM 9/16/2014 Date

***IMPORTANT NOTE:*** *LABORATORY PARTICIPATION IS CONDITIONAL ON YOUR PROVIDING THE NAMES OF THE PATIENTS, AND THE QUANTITY OF TESTS PERFORMED IN CONJUNCTION WITH THE ATTACHED PROTOCOL. THIS WILL BE REQUIRED 90 DAYS FOLLOWING THE START OF THE PROJECT, AND EVERY 90 DAYS THEREAFTER UNTIL COMPLETION OF THE STUDY.*